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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,722	10/06/2003	Duane D. Miller	20609/203 (PD 00034)	2869

7590  
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01/19/2007

EXAMINER

AULAKH, CHARANJIT

ART UNIT

PAPER NUMBER

1625

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/19/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	Application No. 10/679,722	Applicant(s) MILLER ET AL.	
	Examiner Charanjit S. Aulakh	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 06 October 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-44 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-44 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date: _____   | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

1. Claims 1-44 are pending in the application.

#### *Response to Arguments*

2. Applicant's arguments filed on Oct. 6, 2006 have been fully considered but they are not persuasive regarding enablement and indefiniteness rejections. In regard to enablement for treating various disease conditions, the applicants cited an article by Wise and a review article by Philipp et al. However, both of these article do not say anything regarding well known utility of either alpha2a or alpha2c receptor antagonists in treating hypertension, erectile dysfunction, pain, glaucoma, alcohol and drug withdrawal, rheumatoid arthritis, ischemia, migraine, cognitive deficiency, spasticity, diarrhea and nasal congestion. Actually, the review article by Philipp clearly states that " Despite the fact that alpha2-adrenergic receptors serve a number of physiological functions in vivo and have great therapeutic potential, no sufficiently subtype-selective ligands are clinically available yet " ( see page 287, right column ).The only well established utility is for beta2 receptor agonists in asthma and beta1 receptor antagonists in hypertension. In regard to treating atherosclerotic coronary arteries, there is no teaching in Philipp's review article regarding efficacy of alpha2a receptor antagonists. Actually, this article specifically mentions ( page 290, left column ) that it is still unknown which alpha2-receptor subtype is responsible for the vasoconstriction in humans. In regard to sedation and hypotension, Philipp's article clearly teaches that alpha2a receptor agonists and not antagonists mediate these effects and therefore, selective alpha2a receptor antagonists will have utility in treating adrenergic alph2a-

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receptor-mediated hypotension and sedation. In regard to treatment of Raymond's phenomenon, Philipp's article mentions diminishing the vasoconstriction by alpha2-adrenergic antagonists and not by alpha2c receptor antagonists. The study by Wise does show efficacy of OPC-28326 ( with preferential binding to alpha2c receptors ) at high dose in Raymond's phenomenon. However, the structure of this compound is not disclosed and therefore, it is not clear whether this compound is structurally closely related to instant compounds or not? However, if other structurally diverse compounds having alpha2c receptor antagonist activity are also known in the art to be efficacious in Raymond's phenomenon, only then the instant compounds will have enablement for treating Raymond's phenomenon.

In regard to indefiniteness rejections of instant claims 24-44, the examiner does not agree with the applicant's arguments that claims encompass both in vivo and in vitro use. As stated clearly in the last office action, the compounds need to be administered for inhibition in vivo and there is no mention of administering the instant compounds in the instant claims. Also, as mentioned earlier in response to enablement issues, the instant specification does not have enablement for treating adrenergic alpha2c receptor-mediated condition and therefore, it is not clear what is end result for inhibiting alpha2c receptors in vivo? The instant specification is enabling only for inhibiting the activity of both alpha2a and alpha2c receptors in vitro.

### **Conclusion**

3. Rejections under 35 U.S.C. 112, first paragraph and second paragraph are maintained for the reasons of record.

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**4. THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

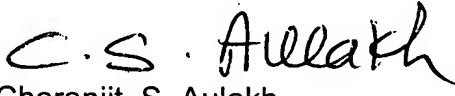
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

**5.** Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on (571)272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
Charanjit S. Aulakh  
Primary Examiner  
Art Unit 1625